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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,644	PLESCH ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16-21,25 and 27-32* is/are pending in the application.

4a) Of the above claim(s) *1, 6-13, 16-21, 25 and 27-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed January 28, 2009 has been entered.

Claims 14-15, 22-24 and 26 are cancelled.

Claims 1, 6-13, 16-21, 25 and 27-30 are withdrawn.

Claims 2 and 5 are currently amended.

Claims 31-32 are new.

Claims 1-13, 16-21, 25 and 27-32 are pending.

Claims 2-5 and 31-32 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5 remain rejected, and claims 31-32 are rejected, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed July 28, 2008.

Applicants' arguments filed January 28, 2009 have been fully considered but they are not persuasive.

Applicants note that claim 2 is not directed to a nucleic acid but rather to a process, a process for the production of fine chemical comprising increasing or generating the expression of a nucleic acid encoding a ras-like GTPase (i.e. SEQ ID NO: 2 and homologues and variants thereof) in an organism or parts thereof. Applicants point out that, as in Example 16 of the Written Description Guidelines (Revision of March 25, 2008), the novelty resides in the method steps and not in the nucleic acids encoding ras-like GTPases. Furthermore, Applicants point out that many ras-like GTPases are known in the art as in Example 16. Applicants maintain, accordingly, that the specification should satisfy the written description for amended claim 2 based on analogy to the examples in the Written Description Guidelines. (reply page 18)

With respect to Applicants' reference to Example 16 in the Guideline Training Material, the facts at issue in the cited example are not analogous to the facts at issue here. Example 16 is directed to a method of introducing a nucleic acid into the mitochondria of mammalian cells where the novelty is in the method steps because the method does not rely on the introduction of any particular type of nucleic acid. In contrast, the claimed method is directed to a method of increasing or generating in an organism or a part thereof the expression of a specific type of nucleic acid molecule, i.e. a nucleic acid molecule encoding the polypeptide as depicted in SEQ ID NO:2, a nucleic acid molecule comprising the nucleotide sequence as depicted in SEQ ID NO:2, a nucleic acid molecule which encodes a polypeptide having at least 70% sequence identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) or (b), a nucleic acid molecule which hybridizes with the nucleic acid molecule of (a) or

(b), or a nucleotide sequence complementary thereto. Accordingly, the novelty of the claimed method is in the method steps. The Examiner further notes that the claims are silent with respect to ras-like GTPases. The only function recited in the claims is the production of fine chemicals in the organism.

Applicants also maintain that the specification provides relevant identifying characteristics of the sequences sufficient to distinguish a ras-like GTPase from other materials, as depicted in Figure 1, conserved regions or domains among ras-like GTPases derived from various organisms, including SEQ ID NO: 2, have been identified. As stated in the specification at page 20, lines 16-20, polypeptides comprising the consensus sequences identified, including SEQ ID NO: 48 and 50, confer an increase of the production of fine chemicals. Applicants maintain, thus, that the genus of molecules has common structure which a skilled artisan would recognize. (reply pages 18-19)

The Examiner reiterates that the claims are silent with respect to ras-like GTPases. The Examiner also maintains that the rejected claims do not require that the encoded polypeptides comprise the conserved regions or domains among ras-like GTPases as depicted in Figure 1. The Examiner additionally maintains that SEQ ID NO: 48 and 50 are not representative species of the genus of sequences recited in the rejected claims.

Applicants also point out that functional homologues and variants of SEQ ID NO: 2 are described in the specification, for example at pages 71-72 and 83, which include natural variations, such as allelic variants or polymorphisms, which can lead to alterations in the amino

acid sequences within a population without altering the functional activity of the ras-like GTPase represented by SEQ ID NO: 2. Applicants maintain, accordingly, that the claim includes the use of the expected range of natural variants, which are certainly within the scope of the invention as the skilled person would envision. (reply page 19)

The Examiner maintains that pages 71-72 and 83 do not describe any actual functional homologues or variants of SEQ ID NO: 2.

Applicants additionally point out that the specification shows, by way of working examples, that the claimed process results in production of fine chemicals in plants when using a nucleic acid encoding a ras-like GTPase (an actual reduction to practice). See Specification at page 189, lines 8-25 (Example 13) and Table 1 at page 174. As summarized in Table 1, where Cols. 3 and 4 provide the ratio of the fine chemicals analyzed between the transgenic and wild-type plants, it is clear that Arabidopsis plants overexpressing YNL090W (i.e. SEQ ID NO: 2) showed an increase in the production of at least 22 fine chemicals. Accordingly, contrary to the Examiner's assertion, the specification describes the actual production (reduction to practice) of fine chemicals in plants. (reply page 19).

The Examiner acknowledges the disclosure at pages 189 and 174, but maintains that the description of a single sequence is not sufficient to describe the broad genus of sequences recited in the rejected claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2, and claims 3-5 dependent thereon, remain rejected, and claims 31-32 dependent thereon are rejected, under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, for the reasons of record set forth in the office action mailed July 28, 2008.

Applicants' arguments filed January 28, 2009 have been fully considered but they are not persuasive.

Applicants note that claim 2 has been amended without prejudice or disclaimer to include a further step of growing the organism to produce the fine chemical. Applicants further note that that methods for increasing or generating expression of a nucleic acid in an organism are well known in the art and routinely employed by one skilled artisan, and are also described in the specification at pages 21-25. Accordingly, it is respectfully submitted that the claims as amended is sufficiently clear and definite in view of the knowledge of the art as well as the disclosure of the specification. (reply page 20)

The Examiner maintains that the amendment of claim 2 does not address the issue of rejection, the absence of a step for increasing or generating in an organism or a part thereof the expression of at least one nucleic acid molecule comprising a nucleic acid molecule. The Examiner also maintains that the knowledge of one skilled in the art regarding methods for increasing or generating expression of a nucleic acid does not remedy the absence of a recitation in the claim of a positive method step by which this may be accomplished, since this method step is essential to the practice of the claimed method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 3 and 5 remain rejected, and claims 31-32 are rejected, under 35 U.S.C. 102(b) as being anticipated by Qadota H. et al. (RHO gene products, putative small GTP-binding proteins, are important for activation of the CAL1/CDC43 gene product, a protein geranylgeranyltransferase in *Saccharomyces cerevisiae*. Yeast. 1992 Sep;8(9):735-41), for the reasons of record set forth in the office action mailed July 28, 2008.

Applicants' arguments filed January 28, 2009 have been fully considered but they are not persuasive.

Applicants maintain that because claim 2 has been amended without prejudice or disclaimer to specify that the fine chemicals produced by the claimed process are selected from amino acids, carbohydrates, vitamins, organic acids, fatty acids, and carotinoids, and because a protein, by its very definition, is not an amino acid, a carbohydrate, a vitamin, an organic acid, a fatty acid, or a carotinoid, Qadota does not anticipate the claims as now amended (reply page 20).

The Examiner maintains that Applicants' assessment of the claim amendment is incorrect. Claim 2 in pertinent part recites "wherein the fine chemical comprises at least one compound selected from the group consisting of amino acids, carbohydrates, vitamins, organic

acids, fatty acids, and carotinoids.". Because a protein, by its very definition, comprises amino acids, Qadota anticipates the claims as now amended.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 4 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Qadota H. et al. (RHO gene products, putative small GTP-binding proteins, are important for activation of the CAL1/CDC43 gene product, a protein geranylgeranyltransferase in *Saccharomyces cerevisiae*. Yeast. 1992 Sep;8(9):735-41) in view of Monaghan E. et al. (Mutations in the Lcb2p subunit of serine palmitoyltransferase eliminate the requirement for the TSC3 gene in *Saccharomyces cerevisiae*. Yeast. 2002 Jun 15;19(8):659-70), for the reasons of record set forth in the office action mailed July 28, 2008.

Applicants' arguments filed January 28, 2009 have been fully considered but they are not persuasive.

Applicants maintain that, as discussed above, Qadota does not teach a process for the production of such fine chemicals, and that because the reliance on Monaghan is that it teaches the steps recited in claim 4, it follows that the combination of Qadota and Monaghan does not render the present invention obvious because the combined teaching does not teach or suggest the production of the specific fine chemicals as now recited in the amended claim 2.

Applicants also note that Qadota focuses on the effect ofRho2 gene product, a small GTP-bind protein, in the activation of geranylgeranyltransferase, a protein involved in post-translational protein prenylation, and that Monaghan, on the other hand, focuses on the effect of Lcb1 and Lcb2 gene products, homologues to the a-oxoamine synthases, in the serine palmitoyltransferase activity, a protein involved in sphingolipid synthesis. Applicants maintain that because there is no connection between Rho2 and Lcbl/Lcb2 and their function in yeast, there is no motivation for one skilled in the art to combine these two references as suggested by the Examiner. (reply page 21).

The Examiner maintains that Applicants' assessment of the claim amendment is incorrect. Claim 2 in pertinent part recites "wherein the fine chemical comprises at least one compound selected from the group consisting of amino acids, carbohydrates, vitamins, organic acids, fatty acids, and carotinoids.". Because a protein, by its very definition, comprises amino acids, Qadota does teach a process for the production of such fine chemicals.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). With respect to Monaghan, the Examiner maintains that the outstanding rejection does not and need not rely on a connection between Rho2 and Lcbl/Lcb2 and their function in yeast in order to render the claimed invention obvious, because the claim is directed to a process of making and selecting mutants of *Saccharomyces cerevisiae*, and Monaghan was cited for teaching such a process.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia Collins/
Primary Examiner, Art Unit 1638

CC